Primary mediastinal giant synovial sarcoma: A rare case report

Gaetano Rea, Francesco Somma, Tullio Valente, Giuseppe Antinolfi, Graziella Di Grezia, Gianluca Gatta

1. Introduction

Synovial sarcoma is a mesenchymal tissue cell tumor that exhibits epithelial differentiation. Most frequently, it arises in the extremities of adolescents and young adults (1), while a primary occurrence in the mediastinum is quite rare (2). Primary mediastinal synovial sarcoma is a malignant tumor, able to invade adjacent organs or give distal metastases. Pathological examination and genetic features are crucial to establish diagnosis, whereas clinical presentation and imaging patterns are often aspecific and misleading. To date, only few reports have focused on mediastinal synovial sarcoma imaging findings. Herein, we report a case of a 13 cm primary mediastinal giant synovial sarcoma, diagnosed in a 56-year-old patient admitted in our Department of Radiology with a six-month history of dyspnea and back pain.

2. Case report

A 56-year-old male presented to our hospital with a six-month history of dyspnea and back pain, without coughing or shortness of breath. Physical examination revealed nothing of significance in the chest and abdominal regions, as well as in the extremities. During a routine workup, chest X-ray in double projection (posterior–anterior and left lateral) revealed
a round mass in the right thoracic cavity, causing a remarkable mediastinal enlargement (Fig. 1). The location of this mass was the middle to posterior mediastinum using a classification by Felson. Then, the patient underwent a whole body multi-detector computed tomography (MDCT, Brilliance CT 16-slice Philips Medical systems, Best, The Netherlands) with i.v. contrast medium, which defined the presence of a 13 cm enhanced mass in the upper-right region of the chest. The lesion appeared as firmly adherent to the lateral mediastinal pleural surface, to the posterior wall of trachea and to the lateral wall of esophagus, and no cleavage was found between the mass and the carina or the right bronchus. Moreover, no sign of pleural effusion or lymphadenopathy was found (Fig. 2a–d). Following, a flexible bronchoscopy was performed, showing an extrinsic compression of the right upper lobe bronchus but the broncho-alveolar lavage (BAL) was negative for malignant cells. Then, the patient underwent thoracotomy, which revealed a large lesion arising from the right costo-vertebral space, not belonging to the lung but adherent to the mediastinal pleura. The histopathological analysis of the excised mass revealed poorly differentiated spindle-like tumor cells arranged in bundles. Despite the lesion had been confirmed as a malignant mesenchymal tumor at pathology, the exact subtype was hard to define. Immunohistochemistry showed strong positive staining for vimentin, cytokeratin 8, cytokeratin 19 and focally positive for cytokeratin 7 and EMA, and negative for CD34, C5/6, calretine and primary pulmonary tumor marker (TTF-1), which combined with the morphological profile confirmed the diagnosis of mediastinal poorly differentiated monophasic synovial sarcoma. The patient is still alive, disease-free, in good health, currently undergoing follow-up.

3. Discussion

Synovial sarcoma has been defined by the World Health Organization (WHO) in 2002 as a type of mesenchymal tissue cell tumor that exhibits epithelial differentiation (2) and represents the third most common soft-tissue sarcoma in adults,
accounting for approximately 10% of soft-tissue sarcomas (3). Men and women are affected equally and the mean age at presentation is 32 years (4). Indeed, this sarcoma is prevalent in adolescents and young adults between 15 and 40 years (5), accounting for less than 2% of all soft tissue sarcomas in patients older than 50 years. Although 85% of synovial sarcomas arises in joint cavities of lower limbs, rare cases may originate elsewhere, including mediastinum (5). Overall, primary mediastinal synovial sarcoma is exceedingly rare. Indeed, in a retrospective study by Bart et al. (6), only 1.4% of the total 3149 soft tissue sarcomas examined were primary mediastinal sarcomas. Among these, synovial sarcoma accounted for only 2%. Despite its rarity, this tumor shows more aggressive clinical behavior than other soft tissue synovial sarcomas. With regard to clinical presentation, primary mediastinal synovial sarcoma often reveals various and aspecific initial symptoms due to compression, such as chest pain, cough, fever, back pain, shortness of breath and dyspnea, which are common findings in many mediastinal tumors. Therefore, it is crucial to combine imaging and pathology to establish the diagnosis. In particular, this neoplasm is characterized by the chromosomal translocation t(4;18)(p11;q110) and is thought to be of totipotential mesenchymal cell origin (7). According to the various histological patterns of epithelial and spindle cells in the mass, synovial sarcoma is divided into four subtypes (8): (1) monophasic fibrous synovial sarcoma, composed of homogeneous spindle cells with pale-staining nuclei arranged in fascicles and sheets, embedded in a variable background of myxoid to densely collagenous elements; (2) monophasic epithelial synovial sarcoma, composed of relatively uniform spindle cells with elongated nuclei, slightly basophilic cytoplasm and indistinct cell borders with tumor cells densely packed and little intervening stroma; (3) biphasic synovial sarcoma, composed of both spindle and epithelial cells; (4) poorly differentiated form. Calcification is a common finding in synovial sarcomas at para-articular sites and can be found in 30% of lesions (1), while has never been described in patients with thoracic lesions (9). Moreover, genetic and immunohistochemistry examinations play a pivotal role in the differential diagnosis of the monophasic form from other stromal tumors, such as fibrosarcoma, hemangiopericytoma, leiomyosarcoma, and the spindle cell variant of squamous cell carcinoma (10–12). Indeed, synovial sarcoma can express mesenchymal markers such as vimentin and the epithelial markers cytokeratin (type AE1/AE3), bcl-2 and/or epithelial membrane antigen (EMA), in combination with CD34 negativity (13,14). In our case, the lesion was confirmed as a malignant mesenchymal tumor at histopathological analysis, but its subtype was hard to individuate. The tumor cells were found to be positive for vimentin, cytokeratin 8, cytokeratin 19 and focally positive for cytokeratin 7 and EMA, and negative for CD34, which, combined with the morphological profile, confirmed the diagnosis of mediastinal monophasic synovial sarcoma (Fig. 3a,b). Nevertheless, in-situ fluorescence hybridization showed in our patient the chromosomal translocation t(x;18)(p11;q110) involving the SYT gene on the long arm of chromosome 18 and the SSX1 or SSX2 gene on the short arm of the X chromosome, which has been demonstrated in more than 90% of synovial sarcomas, regardless of histological subtypes (15). Since this genetic alteration is not associated with other sarcomas, it may be considered as a specific biomarker for diagnosing synovial sarcomas (7). With regard to imaging tools, chest X-ray is usually the first and less accurate exam performed in all thoracic pathologies. Contrary, Multi-Detector Computed Tomography (MDCT) may reveal space-occupying lesions in the mediastinum with no specific radiological pattern to other mediastinal stromal tumors, including necrotic, hemorrhagic or cystic components on section. In particular, on chest radiographs, mediastinal synovial sarcomas may be depicted as a pulmonary parenchymal consolidation or mass (with sharp and ill-defined margins), a pleural-based mass, a focal pleural thickening with or without a central mass or near-complete opacification of the hemithorax (15). There is no propensity for sidedness (15). An ipsilateral pleural effusion may be evident, such as pneumothorax. Anyway, MDCT is much more sensitive in detecting calcified tumor matrix. On MDCT, mediastinal synovial sarcoma typically appears as a well-defined, heterogeneously enhanced mass that contains areas of fluid attenuation compatible with necrosis or hemorrhage (15–17). Likewise in our patient, the reported radiodensity values are 20–40 HU on unenhanced MDCT (9). Mediastinal lymph node enlargement is uncommon (15). The real site of origin (lung, pleura or mediastinum) is often unclear, but acute or recurrent hemothorax and a rim of ground-glass opacity surrounding the mass has been reported in case of pulmonary synovial sarcoma. On Magnetic Resonance Imaging (MRI), compared with soft-tissue sarcoma, mediastinal synovial sarcoma shows less vascularity and a “triple sign” pattern on T2-weighted images, consisting of bright, dark and gray areas, representing the tumor, hemorrhage, and necrosis, respectively (18). Unfortunately, our patient could not undergo MRI because of claustrophobia.

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Fig. 3  Histopathology. Histopathological analysis showing: (a) tumor cells are found to be positive for cytokeratin 8; (b) Ematossilina–Eosin staining (200×) showing poorly differentiated spindle-like tumor cells arranged in bundles.
Mediastinal synovial sarcomas are highly aggressive tumors with a high recurrence rate and ability to progress to metastatic stage. These neoplasms may invade adjacent organs or metastasize via the blood, rarely via the lymphatic system. No sign of distant metastasis or lymph node enlargement became evident during the 2-year follow up in our patient.

Despite the optimal treatment strategy is still unclear due to lack of data of this rare disease, surgery is the treatment of choice in resectable patients (19). For tumors that can be completely excised, surgical resection with or without radiotherapy has been found effective in establishing local control. Patient age, involvement of surgical margins, and tumor size guides the decision about whether additional adjuvant chemotherapy and/or radiotherapy is needed. Certainly, tumor response has occurred with first-line chemotherapy regimens consisting of ifosfamide-based chemotherapy (with or without doxorubicin), however, whether there is a substantial effect on long-term survival is uncertain, and toxicity and side effects must be weighed against potential benefits. Prognosis reported in the poor differentiated forms is poor, but with aggressive multimodal therapy, moderate to high survival has been reported (20). Anyway, any adjuvant chemotherapeutic or radiotherapy was denied by our patient. The overall 5-year survival rate is 50%, and poor prognostic risk factors include age older than 20 years, female sex, incomplete resection, tumor size > 5 cm, extensive tumor necrosis, high number of mitoses (> 10 per 10 high-power fields), neurovascular invasion (21). With the exception of the gender, our patient presented all these poor prognostic risk factors, especially the tumor diameter longer than 13 cm. Also early relapse (< 18 months) has been reported to be significantly associated with worse prognosis, but no relapse has occurred in our patient during the 2-year follow up.

Conflict of interest

The authors declare that they have no conflict of interest.

References